8.592 Term Project: Fixation within a Dynamic Population

Harris H. Wang*
MIT Department of Physics
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Fixation of mutant alleles in the long term can often determine the fate of a population of organisms. In this paper, we studied the probability of fixation of mutant alleles within populations of changing sizes. Specifically, we looked at three population growth patterns: single change, exponential, and logistic. We provided a series of simple formulations to study the dynamics of fixation in response to populations of variable size. Our results show that population size can greatly influence the probability of fixation of both beneficial and deleterious mutant alleles.

1. INTRODUCTION

The ability of a specie to adapt to its environment ultimately depends on its ability to perpetuate beneficial alleles. The perpetuation of specific alleles within a population for many generations is referred to as fixation. Fisher [1, 2], Haldane [3], and Wright [4] proposed the first models to determine the probability of fixation of the beneficial allele within a population and determined that the probability of fixation to be approximately $2s$, where s is the selective advantage of the allele. These models assumed a Poisson distribution of reproductive success and a fixed population. Upon generalizing these models, Kimura [5, 6] solved the Kolmogorov backward equation

$$\frac{\partial u(p,t)}{\partial t} = \frac{V}{2}\frac{\partial^2 u(p,t)}{\partial p^2} + M\frac{\partial u(p,t)}{\partial p}, \tag{1}$$

where

$$M = \lim_{\delta t \to 0} \frac{1}{\delta t}\int (\delta p) f(p, p+\delta P; \delta t) d(\delta p),$$

$$V = \lim_{\delta t \to 0} \frac{1}{\delta t}\int (\delta p)^2 f(p, p+\delta P; \delta t) d(\delta p).$$

The quantity of interest here is the long-term behavior of the fixation probability $u(p) = \lim_{t\to\infty} u(p,t)$. By setting $\partial u/\partial t = 0$ with boundary conditions $u(0) = 0$ and $u(1) = 1$, we can solve Eq. 1 using

$$u(p) = \frac{\int_0^p G(x)dx}{\int_0^1 G(x)dx},$$

where $G(x) = e^{-\int \frac{2M_{\delta x}}{V_{\delta x}dx}}$ in which $M_{\delta x}$ and $V_{\delta x}$ are the mean and variance of the change in gene frequency x per generation.

Using a diffusion approximation, Kimura *et al.* showed that the probability of eventual fixation is

$$\frac{1 - e^{-4N_e sp}}{1 - e^{-4N_e s}},$$

where N_e is the variance effective size of a diploid population size of N and p is the frequency of the beneficial allele. The probability of fixation of a new mulation $p = 1/2N$ within a large population $N_e S \gg 1$ is thus $2sN_e/N$. The model, however, relies on having a population of same average size.

The population size in nature, however, may vary considerably due to various factors such as predator density, resource availability, and habitat and environmental changes. The rate of fixation of alleles will in turn change in response to the population change. Fisher [7] first proposed that the probability of fixation should increase with increasing population and decrease with a shrinking population. Kojima and Kelleher [8] have since then verified Fisher's assertion through numerical simulation.

This paper discusses some of the recent works [9, 10] that have examined changes in probability of fixation in a changing population. Several population growth patterns are presented including single-change, exponential, and logistic. From these results, one can determine the flux of beneficial mutations into a population as well as extend the analysis to study fixation of deleterious mutations.

2. FIXATION WITHIN POPULATION OF CONSTANT SIZE

Assuming that the number of offspring alleles derived from parent allele follows a Poisson distribution with a mean of one, the population size should be approximately constant. An individual with a mutation that gives it patent genotypic or phenotypic advantage over the wild-type will have higher reproductive success; thus it will generate on average $1+s$ times more offsprings, where s measures the relative fitness advantage of the mutant in a haploid population or the relative fitness advantage of the heterozygote in a randomly mating diploid population. If P_t is the probability of fixation of a mutation that appears in generation t, then $1 - P_t$ is the probability of the eventual loss of the allele. The probability of an allele at generation t being lossed in the long run is equal to the probability of having all j offsprings fail to reproduce, $(1 - P_{t+1})^j$, summed over all values of j. For a Poisson distrubtion with mean $1+s$ giving rise to the number of

*Electronic address: harrisw@mit.edu

offsprings carrying the beneficial allele, we have

$$1 - P_t = \sum_{j=0}^{\infty} e^{(1+s)} \frac{(1+s)^j}{j!} (1 - P_{1+t})^j,$$

which is evaluated to give

$$1 - P_t = e^{-(1+s)P_{t+1}}. \quad (2)$$

Haldane [3] assumed that the population size and the selective advantage s are both constant, thus giving rise to the same probability of fixation of the beneficial allele over generations ($P_t = P_{t+1}$). Under these assumptions and neglecting higher order terms, Eq. 2 produces the result $P_t \cong 2s$.

3. FIXATION WITHIN POPULATION OF CHANGING SIZE

Let N_t be the population size at generation t and ΔN_t be the change in population size from generation t to $t+1$. We can modify Eq. 2 to reflect the increase in the average number of offsprings produced after each generation N_{t+1}/N_t or in another form $1 + \Delta N_t/N_t$ to give

$$1 - P_t = e^{-(1+s)(1+\Delta N_t/N_t)P_{t+1}}. \quad (3)$$

This equation, produced by Ewens [11], predicts that the probability of fixation is always higher than $2s$ if the population is growing $\Delta N_t > 0$. Conversely, a decrease in population will decrease the probability of fixation and lead to the eventual loss of the allele.

Assuming small s, P_t, and $(dN_t/dt)(1/N_t)$ and ignoring higher than second order terms, Eq. 3 under the continuous time limit becomes

$$\frac{dP_t}{dt} \cong -P_t \left(s + \frac{dN_t}{dt} \frac{1}{N_t} \right) + \frac{{P_t}^2}{2}, \quad (4)$$

Eq. 4 can also be derived from the diffusion equation [9].

3.1. Single Change in Population Size

We can calculate the change in the probability of fixation of a population that undergoes a single size change. Assume a population with a size N_0 at time $t = T$ suddenly increase or decrease its population size to N_1 at time $t = T+1$ and remains at N_1. Following our previous discussion of Eq. 2, let $P' \cong 2s$ be the probability of fixation for a constant population. Thus, we have $P_{T+1} = P'$ for the constant population size N_1 after $T+1$. Substitution of this result into Eq. 3 and neglecting higher order terms (for small s and P') produces the condition

$$P_T \cong P'(N_1/N_0), \quad (5)$$

which is used to solve Eq. 4 for $dN_t/dt = 0$ to produce

$$P_t \cong P' \frac{N_1}{N_1 + (N_0 - N_1)e^{-s(T-t)}}, \quad (6)$$

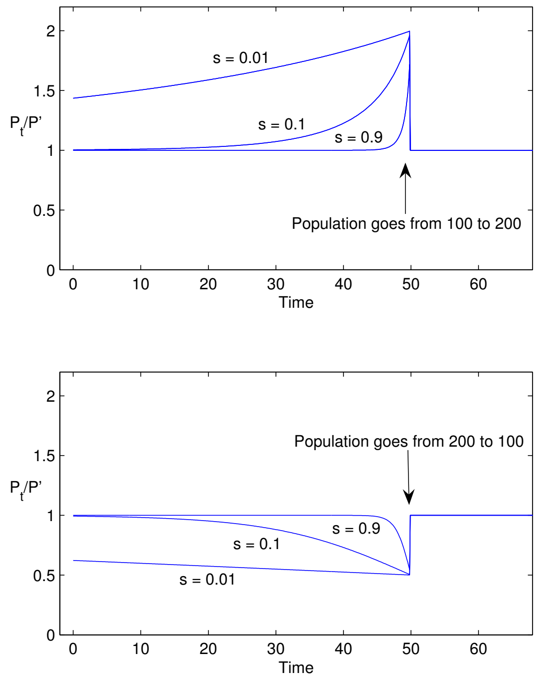

FIG. 1: Changes in probability of fixation within a population undergoing a single change of doubling (top) or halving (bottom). The probability of fixation of alleles with weak selective advantage (small s) are more affected than ones with strong selective advantage.

for $t \leq T$. The ratio of the fixation probabilities are plotted in Figure 1 for various s. We observe that alleles with weak selective advantage have fixation probabilities that are more affected by the single population size change. In addition, a single change in population size backpropagates to affect the fixation probabilities in the previous generations.

3.2. Exponential Population Growth

If the population increases at a constant rate r after every generation, then $r = \Delta N_t/N_t$. Now, instead of $1 + s$ in Eq. 3, we have $(1 + s)(1 + r)$. Taking r to be small, we get $1 + (s + r)$, which produces the probability of fixation

$$P_t \cong 2(s + r). \quad (7)$$

Note that the approximation is useful only for small r and s and for $s + r > 0$. With a higher selective advantage, a mutant allele can withstand a higher rate of exponential population decrease and still hope to survive in the future generations. However if $s + r < 0$, the mutant allele will not fix and will eventually disappear. We note that under exponential growth, the probability of fixation is highly sensitive to the growth rate, especially for weakly selected alleles.

3.3. Logistic Population Growth

Populations cannot grow indefinitely as each environment can only sustain a population upto the limit of its resources, which we will call the carrying capacity C of the environment. In logistic growth, the population increase is density-dependent which means that the population increases at a higher rate if the population is small and at a lower rate if the population is large. When the population reaches the carrying capacity C, the population ceases to grow. Consider the following equation that satisfies the just-mentioned logistic growth criteria

$$\frac{dN_t}{dt} = \left(1 - \frac{N_t}{C}\right) rN_t, \tag{8}$$

which has a solution

$$N_t = C \frac{N_0}{N_0 + (C - N_0)e^{-rt}}, \tag{9}$$

where N_0 is the initial population size and r is the intrinsic logistic growth rate. Substitution of Eq. 8 into Eq. 4 produces

$$\frac{dP_t}{dt} \cong -P_t \left(s + r\left(1 - \frac{N_t}{C}\right)\right) + \frac{{P_t}^2}{2},$$

which using the chain rule can be rewritten as

$$\frac{dP_t}{dN_t} \cong -P_t \frac{(sC + (C - N_t)r)}{N_t r(C - N_t)} + {P_t}^2 \frac{C}{2N_t r(C - N_t)}. \tag{10}$$

We can solve Eq. 10 for P_t in terms of N_t to get

$$P_t \cong \frac{2sC(s + r)}{sC + rN_t}. \tag{11}$$

Note that Eq. 11 reduces to our previous result $2s$ when the population is constant for $N_t = C$ and $2(s+r)$ when the carrying capacity is much larger than the population $C \gg N_t$ as in the exponential growth case. This result can also be obtained using the diffusion model [12].

Since we know N_t for all t from Eq. 9, we can substitute the result into Eq. 11 to get

$$P_t \cong \frac{2s(s + r)(N_0 + (C - N_0)e^{-rt})}{N_0(s + r) + s(C - N_0)e^{-rt}}. \tag{12}$$

Figure 2 plots Eq. 9 and 12 for different values of selective advantage. We see that because the population growth is curbed by the carrying capacity, the probability of fixation will correspondingly decrease to the constant value $2s$ as population approaches the carrying capacity. From this result, we see that the population size N_t and the carrying capacity C have large impact on the probability of fixation P_t.

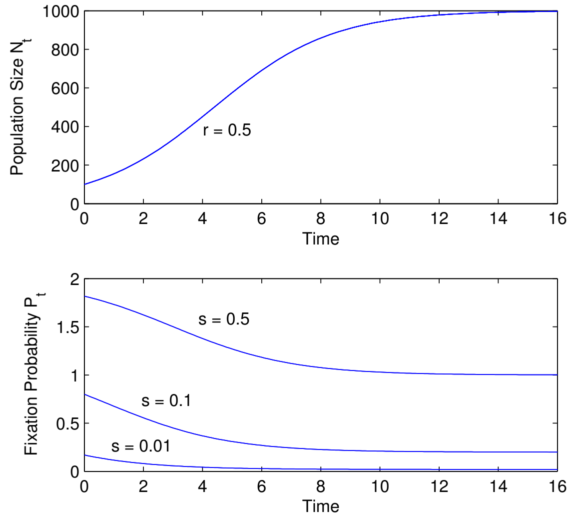

FIG. 2: Changes in probability of fixation within a population undergoing logistic growth. The top figure shows the population as a function of time and the bottom figure shows the probability of fixation as a function of time. The probability of fixation of alleles with weak selective advantage (small s) are is less affected than ones with strong selective advantage. At the long-time limit when the population reaches the carrying capacity, the probability of fixation becomes the constant population limit of $2s$.

4. DISCUSSION

The probability of fixation of a beneficial allele is strongly dependent on population dynamics, in particular changes in population size. In growing populations, the selective advantage of beneficial alleles are amplified, thus allowing for fixation of the beneficial allele to the genome of the specie. Conversely, beneficial alleles are more likely to be lost in a shrinking population. The argument presented here can be extended to study deleterious alleles as well. A deleterious allele will have a negative selective advantage $s < 0$ and thus will exhibit fixation dynamics that are the opposite to that of the beneficial allele. In a growing population, deleterious alleles will have a decrease in probability of fixation and will become extinct in the long run. For a shrinking population, deleterious alleles will have a higher probability of fixation.

From a conservationist viewpoint, the results of the paper are not so optimistic. In shrinking populations of species facing environmental pressures caused by mankind, for example, it would seem that the propagation of beneficial alleles become limited while the propagation of deleterious alleles are enhanced. However, mutant alleles that give an organism particular striking fitness such as resistence to disease, biotic agents, or otherwise toxic chemical, will have a greater chance of fixation even though the population may drastically decrease in the short term.

In this paper, we have outlined a number of growth patterns that may affect the probability of fixation of mutant alleles. The formulations presented can be used to determine the effect of demographic changes on adaptive evolution and the incorporation of new alleles to the genetic pool.

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